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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,574	07/20/2001	Frank A. Skraly	MBX 039	2982

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/909,574	SKRALY ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

The amendment filed on July 8, 2005, amending claims 1 and 10, has been entered.

Claims 1-4 and 6-10 are pending.

Response to Arguments

Applicant's arguments filed on July 8, 2005 have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 6-10 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 and 6-10 are drawn to a method for producing polyhydroxyalkanoates from 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate in plants, wherein the hydroxyalkanoates are produced from any

diols using any diol oxidoreductase and any aldehyde dehydrogenase which are active in bacteria and plants. Although claims 2-4 and 6-7 are limited to specific diols, the hydroxyalkanoates are produced using any diol oxidoreductase and any aldehyde dehydrogenase which are active in bacteria or plants. Therefore, these claims are drawn to a method of using a genus of diol oxidoreductase having any structure which are active in bacteria or plants, a genus of aldehyde dehydrogenase having any structures which are active in bacteria or plants, genus of any plants and/or a genus of any diols. The genus of diol oxidoreductase and the genus of aldehyde dehydrogenase comprise of numerous enzymes that may or may not convert 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol and 1,2-propanediol to its corresponding hydroxyalkanoate. And, a genus of diol oxidoreductase and genus of aldehyde dehydrogenase comprise of numerous enzymes that may or may not convert any diols to 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate. And, any plants may or may not be able to form polyhydroxyalkanoates even if all enzymes recited in the claims are present.

Further, the genus comprising aldehyde dehydrogenase comprise of species that are structurally unrelated and utilize substrates unrelated to the diols listed above (see ExPASy database: aldehyde dehydrogenase). Similarly, the genus comprising diol oxidoreductase comprises of species that are structurally unrelated and utilize substrates unrelated to the diols listed above (See ExPASy database: diol oxidoreductase). The specification only describes a method of producing

polyhydroxyalkanoates from hydroxyalkanoates by converting 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol in bacteria with an aldehyde dehydrogenase (aldH) from *E. coli* and a 1,3-propanediol oxidoreductase (dhaT) from *K. pneumoniae*. Therefore, the specification fails to describe a representative species of the genus of diol oxidoreductase, genus of aldehyde dehydrogenase, genus of plants and genus of diols that are able, in combination, to convert diols to said hydroxyalkanoates.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 1-4 and 6-10.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that from the specification and teachings from the art, one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus of aldehyde dehydrogenase and diol oxidoreductase in view of the species disclosed. Examiner respectfully disagrees. The claims are drawn to a method of using any diol oxidoreductase having any structure and any aldehyde dehydrogenase having any structures. The genus of diol oxidoreductase and the genus of aldehyde dehydrogenase comprise of numerous enzymes, including variants and mutants, that

may or may not convert 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol and 1,2-propanediol to its corresponding hydroxyalkanoate and the genus comprising aldehyde dehydrogenase comprise of species that are structurally unrelated and utilize substrates unrelated to the diols listed above. Therefore, contrary to applicant's arguments, one of skill in the art would not recognize that the applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus of aldehyde dehydrogenase and diol oxidoreductase. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a

genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genus of diol oxidoreductase and genus of aldehyde dehydrogenase include species which are widely variant in structure and substrate specificity. As such, the disclosure solely generic functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

Applicants also argue that the specification teaches primers and oligonucleotides sequences hybridizing to *aldH* and *dhaT* genes and how to isolate gene encoding aldehyde dehydrogenase and diol oxidoreductase from other organisms using said sequences, and therefore, the claimed genes are clearly limited on the requirement for them to be complementary to the primers and/or oligonucleotides disclosed. Examiner respectfully disagrees. The claims do not recite any limitation that the diol oxidoreductase and aldehyde genes hybridize to the primers/oligonucleotides disclosed in the specification. Further, even though some members of the genus of diol oxidoreductase and genus of aldehyde dehydrogenase were known in the art, neither art or the specification describes a method of producing polyhydroxyalkanoates using any diol oxidoreductase and any aldehyde dehydrogenase which are active in bacteria and plants by converting any diols into the recited hydroxyalkanoate monomers. Further, neither art nor specification describes a method of producing polyhydroxyalkanoates in any plants. Production of polyhydroxyalkanoates in plants is limited. Art teaches that production of polyhydroxyalkanoates in plants is complicated because metabolism in plants is compartmentalized (Huisman et al. – form PTO-1449).

Applicants argue that since the claims have been amended to recite that diol oxidoreductase and aldehyde dehydrogenase expressed by the organisms can convert diols into hydroxyalkanoate monomers, the claims are no longer drawn to diol oxidoreductase or aldehyde dehydrogenase having any structure. Examiner respectfully disagrees. While it is true that the claims are now drawn to a method of using diol oxidoreductase and aldehyde dehydrogenase expressed by the organisms which can convert diols into hydroxyalkanoate monomers, the claims remain drawn to a method of using a genus of diol oxidoreductase and aldehyde dehydrogenase having any structure. Further, it is unclear how this new limitation describes the structure of the enzymes.

Claims 1-4 and 6-10 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing polyhydroxyalkanoates from hydroxyalkanoates in bacteria by converting 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol to its corresponding hydroxyalkanote using an aldehyde dehydrogenase (aldH) from *E. coli* and a 1,3-propanediol oxidoreductase (dhaT) from *K. pneumoniae,* does not reasonably provide enablement for a method of producing polyhydroxyalkanoates from hydroxyalkanoates using any or all diol oxidoreductases, any or all aldehyde dehydrogenases by converting any diols to hydroxyalkanoates in any plants. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1 and 8-10 are drawn to a method for producing polyhydroxyalkanoates from 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate in any plant, wherein the hydroxyalkanoates are produced by converting any diols to said hydroxyalkanoates with any diol oxidoreductase and any aldehyde dehydrogenase. While claims 2-7 limit the diols used in the method, said claims continue to encompass the use of any or all aldehyde dehydrogenases which are active in bacteria or plants, diol oxidoreductases which are active in bacteria or plants.

Many different oxidoreductase from the family of diol dehydrogenase are known and many different dehydrogenase from the family of aldehyde dehydrogenases are known (see ExPASY database: aldehyde dehydrogenase and ExPASY database: diol oxidoreductase). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of diol

dehydrogenase, aldehyde dehydrogenase and diols broadly encompassed by the claims.

It would require undue experimentation of the skilled artisan to make and use the claimed method to convert any diols into 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate in any plant using any diol oxidoreductase and any aldehyde dehydrogenase. It would also require undue experimentation of the skilled artisan to make and use the claimed method to convert 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol into 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate or 3-hydroxyhexanoate using any diol oxidoreductase and aldehyde dehydrogenase. The specification is limited to teaching the use of an aldehyde dehydrogenase (aldH) from *E. coli* and a 1,3-propanediol oxidoreductase (dhaT) from *K. pneumoniae* to produce 4-hydroxybutyrate, 2-hydroxybutyrate, 4-hydroxyvalerate, 5-hycroxyvalerage, 6-hydroxyhesanoate, 2-hydroxyethannoate, 2-hydroxypriopionate and 3-hydroxyhexanoate from 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol but provides no guidance with regard to the making of said hydroxyalkanoates with any diols and any diol oxidoreductase and any aldehyde dehydrogenase in any plant. The specification also does not provide guidance with regarding to the making of said hydroxyalkanoates with any diol oxidoreductase and any aldehyde dehydrogenase.

In view of the great breadth of the claim, amount of experimentation required to make the claimed hydroxyalkanote, the lack of guidance, working examples, and unpredictability of the art in predicting which diol oxidoreductase, aldehyde dehydrogenase, plant and/or diol to use, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by the claims.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including method of making hydroxyalkanoates in plants derived from any diols using any diol oxidoreductase and any aldehyde dehdyrogenase and a method of making hydroxyalkanoates derived from 1,6-hexanediol, 1,5-pentaediol, 1,4-butanediol, 1,3-propanediol, 1,2-ethanediol or 1,2-propanediol using any diol oxidoreductase and any aldehyde dehydrogenase. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of which diol oxidoreductase, aldehyde dehydrogenase, plant and/or diols to use is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the specification and the prior art discloses organisms that can be used to produce polyhydroxyalkanoates, diols that may be utilized to form the claimed polyhydroxyalkanoate monomers and diol oxidoreductases and aldehyde dehydrogenases used to convert diols into hydroxyalkanoate monomers. Examiner respectfully disagrees, as discussed above.

Applicants also argue that since methods for cloning genes encoding the above enzymes are well known and such methods are described in the specification, other aldehyde dehydrogenase and diol oxidoreductase can be cloned without undue experimentation. As discussed above, even though some members of the genus of diol oxidoreductase and genus of aldehyde dehydrogenase were known in the art, neither art or the specification describes a method of producing polyhydroxyalkanoates using any diol oxidoreductase and aldehyde dehydrogenase by converting any diols into the recited hydroxyalkanoate monomers. Further, neither art nor specification describes a method of producing polyhydroxyalkanoates in any plants. Production of polyhydroxyalkanoates in plants is limited. Art teaches that production of polyhydroxyalkanoates in plants is complicated because metabolism in plants is compartmentalized (Huisman et al. – form PTO-1449).

Applicants argue that since the claims have been amended to recite that diol oxidoreductase and aldehyde dehydrogenase expressed by the organisms can convert diols into hydroxyalkanoate monomers, one of ordinary skill in the art would not select an enzyme that cannot perform this function. While it is true that the claims are now drawn to a method of using diol oxidoreductase and aldehyde dehydrogenase

expressed by the organisms which can convert diols into hydroxyalkanoate monomers, it would require undue experimentation of the skilled artisan to practice the claimed method, which encompasses converting any diols into the recited hydroxyalkanoate monomers using any diol oxidoreductase and any aldehyde dehydrogenase in any plant. In view of the great breadth of the claim, amount of experimentation required to make the claimed hydroxyalkanote, the lack of guidance, working examples, and unpredictability of the art in predicting which diol oxidoreductase, aldehyde dehydrogenase, organism and/or diol to use, the claimed invention would require undue experimentation.

Applicants also argue that there is no legal requirement that all of the enzymes within the scope of the claims convert the diols to their corresponding hydroxyalkanoate monomers for the enzymes to have the specified utility since "even if some of the claimed combinations were inoperative, the claims are not necessarily invalid" and it would only take routine experimentation to identify other aldehyde dehydrogenase and diol oxidoreductase that can convert the diols into their corresponding hydroxyalkanoates. Examiner respectfully disagrees. As discussed above, it would require undue experimentation of the skilled artisan to determine which specific set of enzymes from among the extremely large groups of enzymes as encompassed by the claims do actually work in order to practice the claimed method, which encompasses converting any diols into the recited hydroxyalkanoate monomers using any diol oxidoreductase and any aldehyde dehydrogenase in any plant.

None of the claims are allowable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Examiner 1652